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(71) Applicant *(for all designated States except US)*: **OXFORD INSTRUMENTS PLC** [GB/GB]; Old Station Way, Eynsham, Witney, Oxon OX8 1TL (GB).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **HANLEY, Peter** [GB/GB]; Western Lodge, Parkend, Lydney, Gloucestershire GL15 4JQ (GB).

(74) Agent: **GILL JENNINGS & EVERY**; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB).

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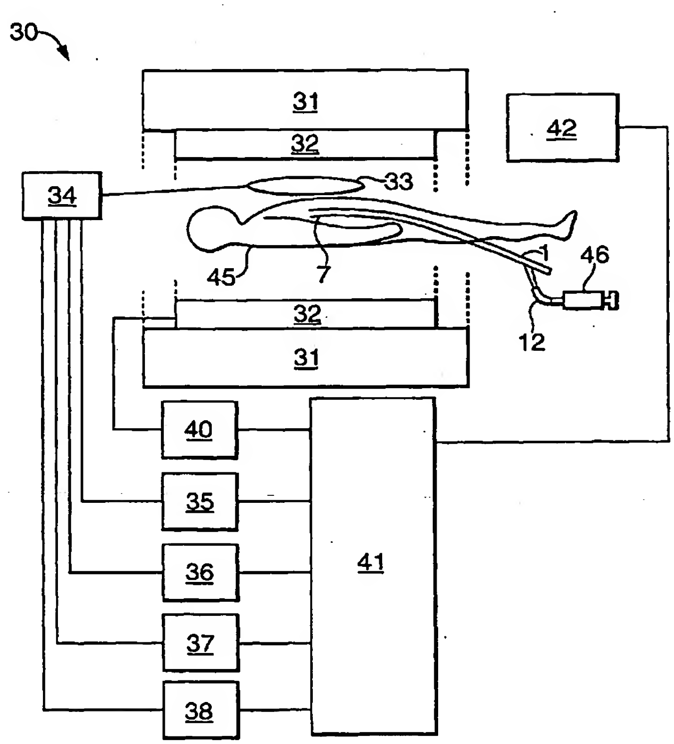
(54) Title: MONITORING THE POSITION OF A MEDICAL INSTRUMENT INSERTED INTO THE BODY OF A SUBJECT USING NUCLEAR MAGNETIC RESONANCE IMAGING



(57) Abstract: A nuclear magnetic resonance imaging system (30) for use in monitoring the position of a medical instrument inserted within the body of a subject. The system comprises: a nuclear magnetic resonance imaging device (31-42) ; a medical instrument (1) for inserting into the body of a subject, the medical instrument having a conduit for supplying a hyperpolarised gas to a region within and/or adjacent the medical instrument; and a hyperpolarised gas supply system (46) for supplying the hyperpolarised gas to the medical instrument.

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MONITORING THE POSITION OF A MEDICAL INSTRUMENT INSERTED INTO THE BODY OF A SUBJECT, USING NUCLEAR MAGNETIC RESONANCE IMAGING

The present invention relates to a method and apparatus for Magnetic Resonance Imaging (MRI) and more specifically to the imaging of medical devices when inserted within the body of a subject.

The accurate localisation of a medical device within the body of a subject is problematical when using MRI. The device can be expected to make several contributions to the image and these are particularly dependent upon the type of material from which the device is constructed.

For example, if the device is metallic, then the absence of Radio Frequency (RF) fields within it and the reduction in RF field strength in its vicinity, will lead to a null signal from the device and a reduced and noisy signal from the region surrounding it.

If the device is constructed from a solid material, then the absence of mobile hydrogen nuclei (protons) will also lead to a null signal.

For small devices, the size of the null signal artefact will be comparable to the pixel size, and this will make it difficult to see. In any case, it is most likely that the device is smaller than the slice thickness, so that the contrast in this case will be low. The device will also not necessarily lie in the plane of the imaging slice, so a recognisable shape will not necessarily be seen.

The device will also produce a susceptibility artefact resulting from the local B_0 field inhomogeneity caused by the difference in magnetic susceptibility between the device and its surroundings. This results in geometric distortion due to mismapping in the frequency encoding, and signal loss due to "de-phasing".

The strength and nature of the susceptibility artefact depends upon a number of factors and these include:-

i) The difference in magnetic susceptibility between the device and its surroundings;

ii) The size and shape of the device.

iii) The device orientation relative to the B_0 field direction; and

iv) The imaging pulse sequence used, for example:

a) Gradient echoes lead to stronger susceptibility artefacts;

b) Spin echoes lead to weaker susceptibility artefacts; and

c) The pulse sequence which optimises the effect of the device may not be ideal for revealing the surrounding anatomy.

The above problems apply to a number of devices such as guide-wires or metal-braided catheters. However, if the device is a plastic catheter, it may not appear in the MRI image at all.

From the above it can be seen that there is considerable difficulty in not only visualising a medical device by MRI, but also in relating its position to the surrounding anatomy.

One approach to making plastic catheters more visible is to fill the lumen of the catheter with an NMR relaxation agent, such as a dilute solution of a gadolinium chelate. A T_1-weighted image then shows the catheter more clearly. However, as the NMR-relaxation "contrast agent" emerges from the catheter, it eventually reduces the T_1 of the surroundings, and so the contrast is lost.

Another approach is the use of an "active catheter". In this case, the surgical tool is fitted with an RF coil, or antenna, which is connected via a screened lead to a separate receiver channel in the imaging instrument. This receives NMR signals from its immediate surroundings, and this signal can be processed in the usual way. The result is superimposed on a "road map" image acquired from the usual receiver in order to highlight the position of the device.

Alternatively, the system can derive the position of the device and place a corresponding marker on the "road

map" image. This technique identifies its position, but not its orientation. To address this problem, several antennae can be fitted.

From the forgoing, it can be seen that the imaging of guide-wires, catheters and other surgical devices, and the use of such images to relate their position to the surrounding anatomy encounters many problems.

In accordance with a first aspect of the present invention we provide a method of monitoring the position of a medical instrument that has been inserted within the body of a subject, using nuclear magnetic resonance imaging, the method comprising:

introducing a hyperpolarised gas into a region within and/or adjacent the medical instrument; and

imaging the hyperpolarised gas using a nuclear magnetic transmit/receive system to monitor the position of the medical instrument.

The introduction of a hyperpolarised gas into the region within or around the instrument allows its position to be accurately determined. The hyperpolarised gas can be readily imaged using MRI and therefore position information can be determined despite the instrument possibly being located in a lumen containing little imageable material. The position in this case refers to not only the instrument location but also its orientation.

The use of hyperpolarised gases is advantageous over other fluids in that they exhibit a decay in hyperpolarisation (and therefore MRI signature) as a function of time. The time constant of this decay is dependent upon the particular gas used and its environment. Examples of these gases include the isotopes 3-helium and 129-xenon.

A hyperpolarisation decay is beneficial in that it prevents extended regions within a lumen developing a strong MRI response and therefore the newly introduced gas within or around the instrument allows its position to be determined more readily. Although the hyperpolarised

species are described as a "gas", this term is intended to include dissolved gases and microbubbles suspended in a medium.

Typically the hyperpolarised gas is supplied to the region through a conduit arranged within or attached to the body of the medical instrument. In the case of instruments such as catheters, which contain a bore for the transport of fluids, the bore itself may be used as the conduit. Alternatively a separate conduit may be used for example formed within the body of the instrument, or attached to an outer surface.

This technique may be used for the accurate positioning of instruments in procedures such as during biopsies or the placement of stents.

Depending upon the application, it may be convenient to use the gas in gaseous form whereas it may be alternatively supplied dissolved in a synthetic plasma such as a perfluorocarbon blood plasma.

The hyperpolarised gas may be imaged directly with suitable MRI apparatus arranged to image at the gas resonance frequency, such as 11.77MHz/Tesla for 129-xenon. Another possibility is to image the gas using only the hydrogen nucleus (proton) frequency (42.58MHz/Tesla) and in this case relying upon the Nuclear Overhauser Effect in which the polarisation of the gas is transferred to surrounding protons. This effect therefore enhances the proton polarisation in the neighbourhood of the medical instrument, resulting in improved imaging.

Typically therefore, the imaging of the hyperpolarised gas may be performed by transmitting radio frequency signals at the nuclear magnetic resonance frequency of the hyperpolarised gas, and receiving corresponding radio frequency signals at the nuclear magnetic resonance frequency of the hyperpolarised gas and/or hydrogen. Preferably, suitable processing of the received radio frequency signals may be performed to produce corresponding images which may be displayed on a display.

A particular benefit is obtained by imaging at the hyperpolarised gas resonance frequency and at the hydrogen resonance frequency, as this provides more information for analysis. Typically, when the imaging is performed at the nuclear magnetic resonance frequencies of the hyperpolarised gas and hydrogen, the method further comprises displaying the images obtained at each frequency on a display. Preferably the corresponding images obtained may be superimposed on the display to assist in monitoring the position of the medical instrument.

In this case data at both frequencies are preferably acquired concurrently using the same imaging device, so that there is no mis-registration due to motion artefacts. When imaging of the hyperpolarised gas is effected by imaging at the proton frequency only, there would be no distinction between image collection and device localisation, which reduces the possibility of registration errors.

Further information may also be provided by imaging the region by transmitting and receiving radio frequency signals at the nuclear magnetic resonance frequency of hydrogen, prior to the step of introducing the hyperpolarised gas into the region.

In accordance with a second aspect of the present invention, we provide a nuclear magnetic resonance imaging system for use in monitoring the position of a medical instrument inserted within the body of a subject, the system comprising:

a nuclear magnetic resonance imaging device;

a medical instrument for inserting into the body of a subject, the medical instrument having a conduit for supplying a hyperpolarised gas to a region within and/or adjacent the medical instrument; and

a hyperpolarised gas supply system for supplying the hyperpolarised gas to the medical instrument.

Typically the nuclear magnetic resonance imaging device has a transmit/receive system arranged to transmit and receive radio frequency signals at one or more of:-

i) a nuclear magnetic resonance frequency of the hyperpolarised gas; and

ii) a nuclear magnetic resonance frequency of hydrogen. Preferably the transmit/receive system is arranged to transmit and receive signals at the resonance frequencies of the hyperpolarised gas and hydrogen. This may be achieved in a number of ways.

For example the transmit/receive system may comprise a double-tuned coil and tuning circuit for transmitting and receiving radio frequency signals at the nuclear magnetic resonance frequencies of the hyperpolarised gas and hydrogen. The coil therefore acts as a transmitter and receiver at each of the hyperpolarised gas and hydrogen resonance frequencies.

Alternatively a multiple coil system may be used such that the transmit/receive system comprises a first coil and first tuning circuit for transmitting and receiving radio frequency signals at the nuclear magnetic resonance frequency of hydrogen, and a second coil and second tuning circuit for transmitting and receiving radio frequency signals at the nuclear magnetic resonance frequency of the hyperpolarised gas. In this case, for a two coil system, each coil is operated as a transmitter and receiver.

In an alternative multiple coil system, the transmit/receive system may comprise a double-tuned first coil and a first tuning circuit for transmitting radio frequency signals at the nuclear magnetic resonance frequencies of hydrogen and the hyperpolarised gas, and a second double-tuned coil and a second tuning circuit for receiving radio frequency signals at the nuclear magnetic resonance frequencies of hydrogen and the hyperpolarised gas.

Preferably in the case of double coil systems, the first and second coils are arranged such that their axes

are substantially orthogonal to each other and also substantially orthogonal to the magnetic field.

When the transmit/receive system is adapted to operate at the nuclear magnetic resonance frequencies of the hyperpolarised gas and hydrogen, the system preferably further comprises a display for displaying nuclear magnetic resonance images obtained at these frequencies. A suitable processor may be used to control the operation of the nuclear magnetic resonance imaging system.

The hyperpolarised gas supply system is adapted to provide the gas to the medical instrument in a suitably hyperpolarised state. The gas may be hyperpolarised by any known method. These include optical pumping, and low temperature/high magnetic field methods.

In accordance with a third aspect of the present invention, we provide a medical instrument for use with the nuclear magnetic resonance system according to the second aspect of the present invention, wherein the conduit is arranged within or attached to the body of the medical instrument. In order to supply the gas to the region within and/or surrounding the instrument, the conduit typically has at least one opening. The at least one opening is preferably arranged at or adjacent a distal end of the instrument such as a catheter.

It will be appreciated that the positioning of such openings may be dependent upon the medical instrument in question and therefore these may not be at the distal end of such an instrument in all cases.

Preferably, when a catheter is in the form of a tube, the conduit is formed as a second tube arranged coaxially with the first tube.

Some examples of a method and apparatus according to the invention will now be described with reference to the accompanying drawings, in which:-

Figure 1 is a schematic representation, partly in section, of a catheter;

Figure 2 shows an example of a nuclear magnetic resonance imaging system according to the invention;

Figure 3A shows an example of a transmit/receive system having a double tuned transmit and receive coil;

Figure 3B shows an alternative example of a transmit/receive system having two single-tuned coils;

Figure 3C shows a further alternative example of a transmit/receive system having two double-tuned coils; and,

Figure 4 is a flow diagram of a method according to the invention.

Figure 1 shows a catheter 1 for use within the body. In the present example the catheter 1 is a cardiac catheter and comprises inner 2 and outer 3 coaxial tubes, with the inner tube 2 having a bore 4. Each tube is approximately circular in cross-section, with the diameter of the outer tube 3 being sufficiently larger than that of the inner 2 to produce an annular bore 5 formed from the elongate region between the tubes. The catheter is constructed from a suitable material such as a plastics material or an MRI compatible metal such as a titanium alloy or non-magnetic stainless steel.

The inner tube 2 terminates in a narrowing section having an opening 6 at a distal end 7 of the catheter. Similarly, the outer tube 3 narrows at the distal end 7 and terminates in an opening 8.

The catheter 1 is generally elongate and at a proximal end 10 the outer tube 3 terminates in a gas entry port 11 which is arranged for attachment to a gas supply line 12. The gas entry port 11 projects in a directional normal to the elongate axis of the catheter 1, whereas the inner tube 2 projects further along the elongate direction for access by other instruments, or fluid access/drainage along the inner tube bore 4.

A guide wire 15 is also indicated in Figure 1 and this passes through the catheter 1, along the bore 4 within the tubes 2 and 3 and out of the distal end.

In addition to the opening 8 at the end of the outer tube, a number of openings 16 are provided in the outer wall of the outer tube 3, these openings 16 providing communication between the annular bore 5 and the external environment, for example that of a body lumen.

The main function of the outer tube 3 is to supply a hyperpolarised gas to the distal end 7 of the catheter 1. In use, the gas is provided through the supply line 12 and it then passes along the outer tube 3 of the catheter 1 as indicated by the arrows 20. The gas then leaves the outer tube 3 passing through the openings 16 and the opening 8 at the distal end 7 of the catheter 1.

Figure 2 shows a magnetic resonance imaging (MRI) system 30 which includes the catheter 1 described above. The system has a magnetic resonance imaging magnet 31 arranged in a standard cylindrical configuration. Within this MRI magnet are positioned gradient coils 32 and one or more radio frequency (RF) coils 33 (only one shown in Figure 2). In this example, the RF coils 33 are connected to a double tuning circuit 34 and this in turn is connected to a proton frequency transmitter 35, a proton frequency receiver 36, a 129-xenon frequency transmitter 37 and a 129-xenon frequency receiver 38. The proton frequency transmitter and receiver 35,36 operate the RF coil 33 at the proton resonance frequency. Similarly, the 129-xenon frequency transmitter and receiver 37,38 are responsible for the RF coil operation at the 129-xenon resonance frequency.

A power supply 40 for the gradient coils is also indicated. This power supply 40 and the respective transmitter and receiver coils 35-38 are each connected to an MRI console 41 which contains a processor and related systems for the operation of the MRI system 30. A display 42 is also connected to the MRI console 41. This display is used to present the images produced at either or both of the proton and xenon frequencies to the surgeon as well as the system operator.

A subject 45 is shown positioned within the MRI system 30 at the centre of the MRI magnet 31 and gradient coils 32. Figure 2 also illustrates the positioning of the catheter 1 within the subject 45, the distal end 7 being within the body of the subject and the proximal end 10 being positioned externally. A solution injector 46 is connected to the supply line 12 of the catheter. This allows the introduction of a perfluorocarbon synthetic plasma containing dissolved hyperpolarised 129-xenon into the outer tube 3 of the catheter, the solution injector 46 acting as a temporary store for the hyperpolarised gas prior to being supplied to the catheter 1.

In the present example as indicated in Figure 2, a double tuned single coil system is used to transmit and receive the RF signals at both the proton and xenon resonance frequencies. This is shown in more detail in Figure 3A. The RF coil 33 is schematically indicated connected to the double tuning circuit 34. Proton frequency transmission and receiving lines 60 and 61 respectively are shown, as are the corresponding 129-xenon frequency transmission and receiving lines 62 and 63 respectively. As can be seen from Figure 3A, the B_0 field indicated at 65, is positioned normal to the axis of the RF coil 33. The coil produces a magnetic field normal to the B_0 field direction 65.

A second example of the RF coil system is shown in Figure 3B. Here, separate single-tuned RF coils 66,67 are provided for operating at the proton and xenon frequencies respectively. Each of these has an axis orthogonal to the B_0 field 65, with the axis of these two coils 66,67 also being mutually orthogonal. The double tuning circuit 34 of the first example is replaced by separate tuning circuits 68 and 69 for the proton and xenon frequencies respectively.

A third example is shown in Figure 3C, in which separate double tuned coils are provided for transmission 70 and receiving 71 respectively. The transmission coil 70

is connected to a transmission circuit 72, this circuit being double-tuned to cause the RF coil 70 to transmit signals at the proton and xenon frequencies. A receiving coil 71 and corresponding receiving circuit 73 is double-tuned to receive the RF signals at each of the proton and xenon frequencies respectively. As can be seen from Figure 3C, the coils 70 and 71 are arranged having mutually orthogonal axes and each are also orthogonal to the B_0 field direction 65.

The choice of these alternative configurations will depend on factors such as the anatomical and geometric considerations of the procedure, and on the relative sensitivities of the signals from the two nuclear species.

The operation of the magnetic resonance imaging system according to the first example will now be described with reference to Figure 4.

At step 80, the cardiac catheter 1 is inserted within the body of the subject 45 at a suitable location (such as into the femoral artery) and is guided along a previously inserted guide wire 15. The guide wire 15 is not essential and may be used for certain procedures. In this example, the catheter is moved towards the heart of the subject 45. The solution injector 46 is also coupled to the supply line 12 of the catheter, the solution injector 46 being filled with the perfluorocarbon synthetic blood plasma containing hyperpolarised 129-xenon in solution.

At step 81, the subject is positioned between the MRI magnets 31 of the imaging system 30. The imaging system 30 is then operated at step 82 in order to establish the approximate position of the distal tip 7 of the catheter 1. To achieve this, the console 41 is operated by the system operator to perform imaging at the proton and xenon frequencies. During imaging, the gradient coils 32 are controlled in order to allow imaging of particular slices of the subject 45. The processor within the console 41 processes the signals obtained by the proton and xenon frequency receivers 36 and 38, and displays the

corresponding images on the display 42. The image according to either frequency may be displayed at any time and these images may be conveniently superposed in order to provide further detail, for example by assigning a specific colour to each frequency image.

At step 83, the solution injector 46 is operated and the perfluorocarbon solution is passed through the supply line 12 of the catheter and into the outer tube 3 of the catheter 1. As shown in Figure 1, this then passes up the outer tube 3 of Figure 1 and exits through openings 16 and 8 in the region of the distal end 7 of the catheter.

The emerging xenon acts as a marker for the distal end 7 of the catheter. As it becomes visible to the MRI system 30, the corresponding image is displayed on the display 42. This allows accurate determination of the position of the distal end 7 of the catheter, this position including its orientation.

In some cases, for example where the catheter is made of a plastics materials, it may also be possible to image the gas within the catheter itself. This is advantageous in that it provides further information as to the precise location of the distal end 7 of the catheter.

By introducing the plasma solution at a sufficient flow rate, a suitable amount of hyperpolarised gas will be present around the end of the catheter. In such a solution, the polarisation has a decay time constant of the order of 10 seconds. Because the polarisation decays relatively quickly, there is no build-up in the surroundings and contrast is not lost (as would be the case for a relaxation agent, such as gadolinium).

The 129-xenon is dispersed away from the distal end 7 either due to the bulk transport of fluid such as blood or due to general diffusion processes. In either case, the decay of the xenon hyperpolarisation over time will produce a smaller resonance signal and therefore the distal end of the catheter 7 may be imaged successfully.

The enhanced imaging of the distal end 7 of the catheter allow its position to be further adjusted at step 84. Further controlled additions of synthetic plasma may be introduced and the position adjusted iteratively by repeating steps 83 and 84 until the satisfactory position has been established.

Further information may also be obtained by performing a proton MRI imaging operation in the region of interest in addition to the above procedure, for example prior to the introduction of the hyperpolarised gas. This can be performed using the magnetic resonance imaging system 30 by transmitting and receiving radio frequency signals at the proton resonance frequency.

When the catheter has been correctly located, further conventional instruments or catheter procedures may be used, at step 85.

The controlled introduction of hyperpolarized gas into a location around the catheter may also be used in the study of flow of bodily fluids within body lumens for example by introducing plasma at a constant rate and imaging the hyperpolarised gas.

CLAIMS

1. A method of monitoring the position of a medical instrument that has been inserted within the body of a subject, using nuclear magnetic resonance imaging, the method comprising:

introducing a hyperpolarised gas into a region within and/or adjacent the medical instrument; and

imaging the hyperpolarised gas using a nuclear magnetic resonance system to monitor the position of the medical instrument.

2. A method according to claim 1, wherein the imaging of the hyperpolarised gas comprises transmitting radio frequency signals at the nuclear magnetic resonance frequency of the hyperpolarised gas, and receiving corresponding radio frequency signals at the nuclear magnetic resonance frequency of the hyperpolarised gas and/or hydrogen.

3. A method according to claim 2, wherein the imaging of the hyperpolarised gas, further comprises processing the received radio frequency signals to produce corresponding images.

4. A method according to claim 3, when the imaging is performed at the nuclear magnetic resonance frequencies of the hyperpolarised gas and hydrogen, the method further comprising displaying the images obtained at each frequency on a display.

5. A method according to claim 4 wherein the displayed images are superimposed on the display.

6. A method according to any of claims 3 to 5, further comprising imaging the region by transmitting and receiving radio frequency signals at the nuclear magnetic resonance frequency of hydrogen, prior to the step of introducing the hyperpolarised gas into the region.

7. A method according to claim 6, further comprising displaying on the display an image corresponding to the radio frequency signals transmitted and received at the

nuclear magnetic resonance frequency of hydrogen prior to the introduction of the hyperpolarised gas.

8. A method according to any of the preceding claims, wherein the hyperpolarised gas is supplied to the region through a conduit arranged within or attached to the body of the medical instrument.

9. A method according to any of the preceding claims, wherein the hyperpolarised gas is dissolved in a synthetic plasma.

10. A method according to any of the preceding claims, wherein the hyperpolarised gas is xenon-129 or helium-3.

11. A method according to any of the preceding claims, wherein the medical instrument is a catheter.

12. A nuclear magnetic resonance imaging system for use in monitoring the position of a medical instrument inserted within the body of a subject, the system comprising:

a nuclear magnetic resonance imaging device;

a medical instrument for inserting into the body of a subject, the medical instrument having a conduit for supplying a hyperpolarised gas to a region within and/or adjacent the medical instrument; and

a hyperpolarised gas supply system for supplying the hyperpolarised gas to the medical instrument.

13. A system according to claim 12, wherein the nuclear magnetic resonance imaging device has a transmit/receive system arranged to transmit and receive radio frequency signals at one or more of:-

i) a nuclear magnetic resonance frequency of the hyperpolarised gas; and

ii) a nuclear magnetic resonance frequency of hydrogen.

14. A system according to claim 13, when the transmit/receive system is arranged to transmit and receive signals at the resonance frequencies of the hyperpolarised gas and hydrogen, wherein the transmit/receive system comprises a double-tuned coil and tuning circuit for transmitting and receiving radio frequency signals at the

nuclear magnetic resonance frequencies of the hyperpolarised gas and hydrogen.

15. A system according to claim 13, when the transmit/receive system is arranged to transmit and receive signals at the resonance frequencies of the hyperpolarised gas and hydrogen, wherein the transmit/receive system comprises a first coil and first tuning circuit for transmitting and receiving radio frequency signals at the nuclear magnetic resonance frequency of hydrogen, and a second coil and second tuning circuit for transmitting and receiving radio frequency signals at the nuclear magnetic resonance frequency of the hyperpolarised gas.

16. A system according to claim 13, when the transmit/receive system is arranged to transmit and receive signals at the resonance frequencies of the hyperpolarised gas and hydrogen, wherein the transmit/receive system comprises a double-tuned first coil and a first tuning circuit for transmitting radio frequency signals at the nuclear magnetic resonance frequencies of hydrogen and the hyperpolarised gas, and a second double-tuned coil and a second tuning circuit for receiving radio frequency signals at the nuclear magnetic resonance frequencies of hydrogen and the hyperpolarised gas.

17. A system according to claim 15 or claim 16, wherein the first and second coils are arranged such that their axes are substantially orthogonal with respect to each other and are each substantially orthogonal to the magnetic field.

18. A system according to any of claims 13 to 17, further comprising a display for displaying nuclear magnetic resonance images obtained at the nuclear magnetic resonance frequencies of hydrogen and the hyperpolarised gas.

19. A system according to any of claims 12 to 18, wherein the hyperpolarised gas supply system includes hyperpolarising apparatus.

20. A medical instrument for use with a system according to any of claims 12 to 19 , wherein the conduit is arranged within or attached to the body of the medical instrument.

21. An instrument according to claim 20 wherein at least one opening is arranged at or adjacent a distal end of the instrument.

22. A medical instrument according to claim 20 or claim 21, wherein the instrument is a catheter.

23. A medical instrument according to claim 22, wherein the catheter is in the form of a tube and wherein the conduit is a second tube arranged coaxially with the first tube.

Fig.1.

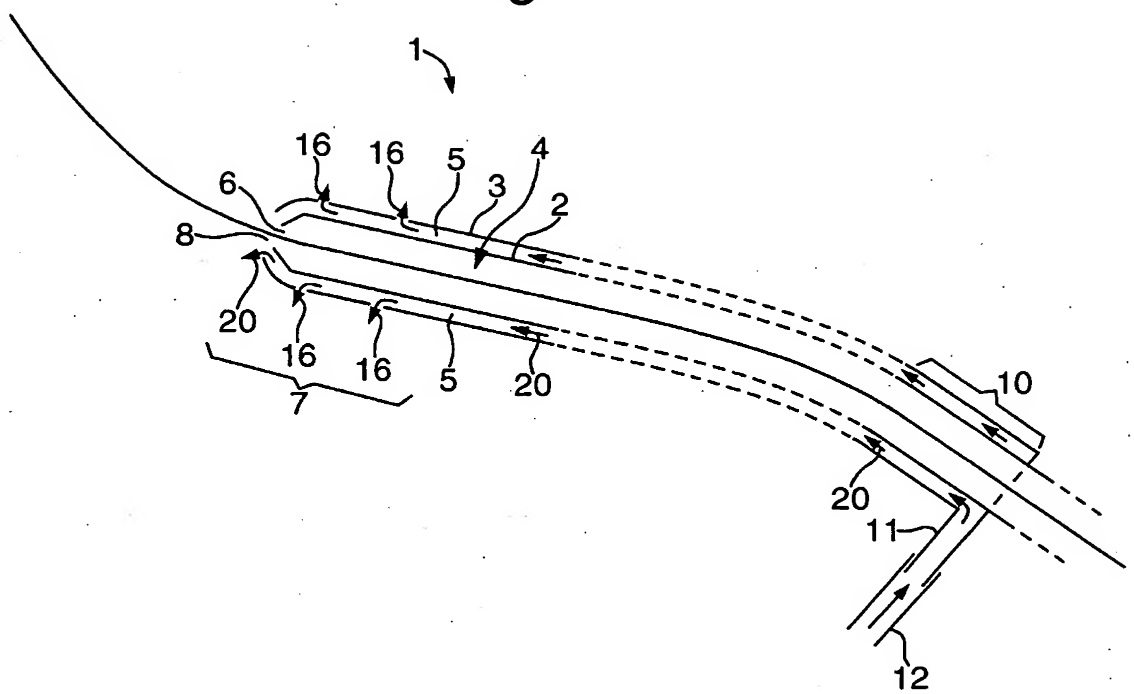


Fig.2.

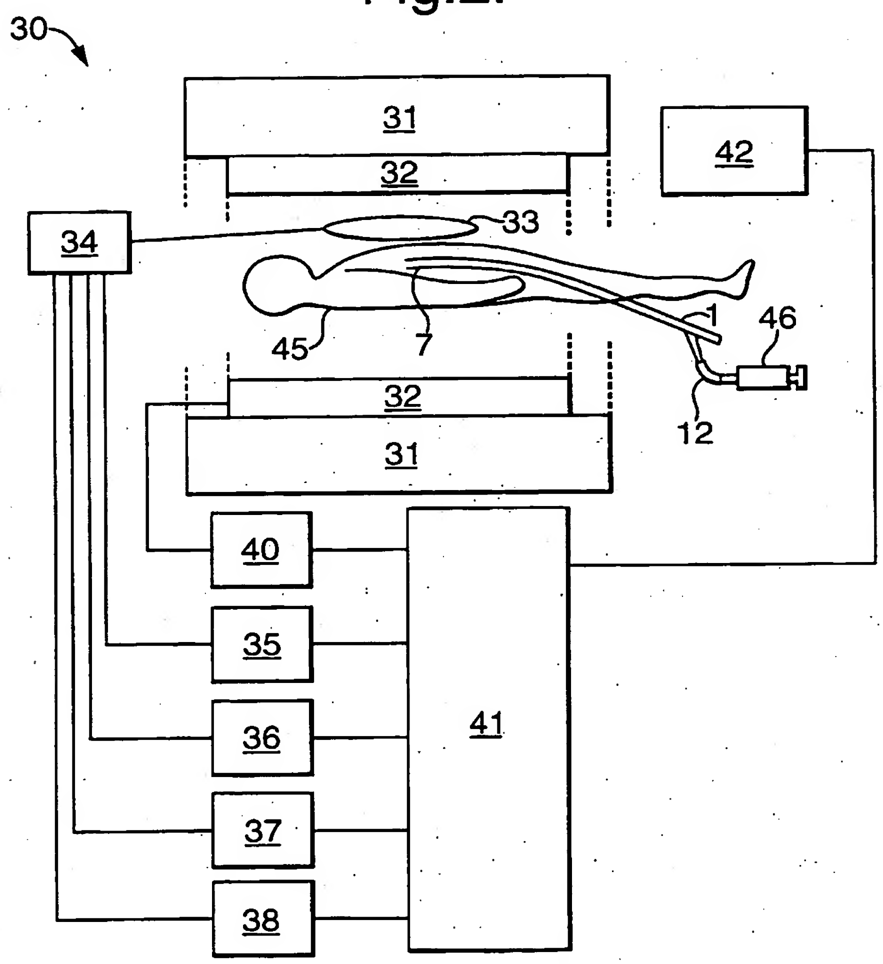


Fig.3A.

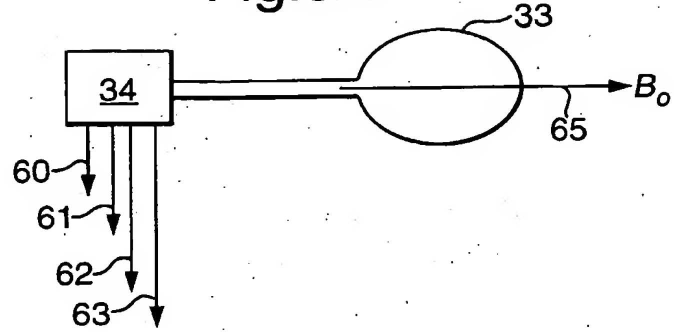


Fig.3B.

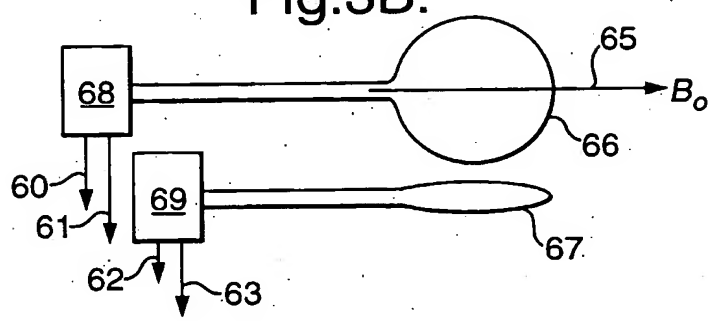


Fig.3C.

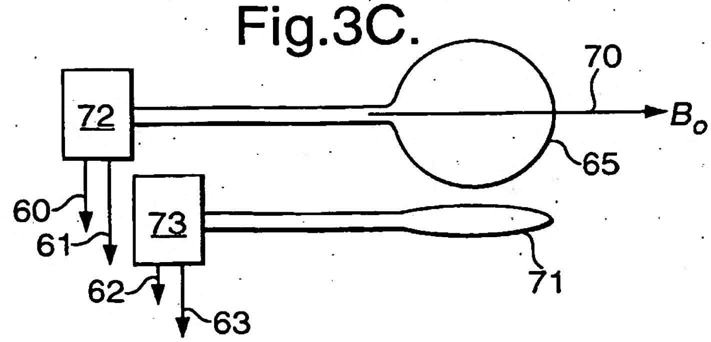
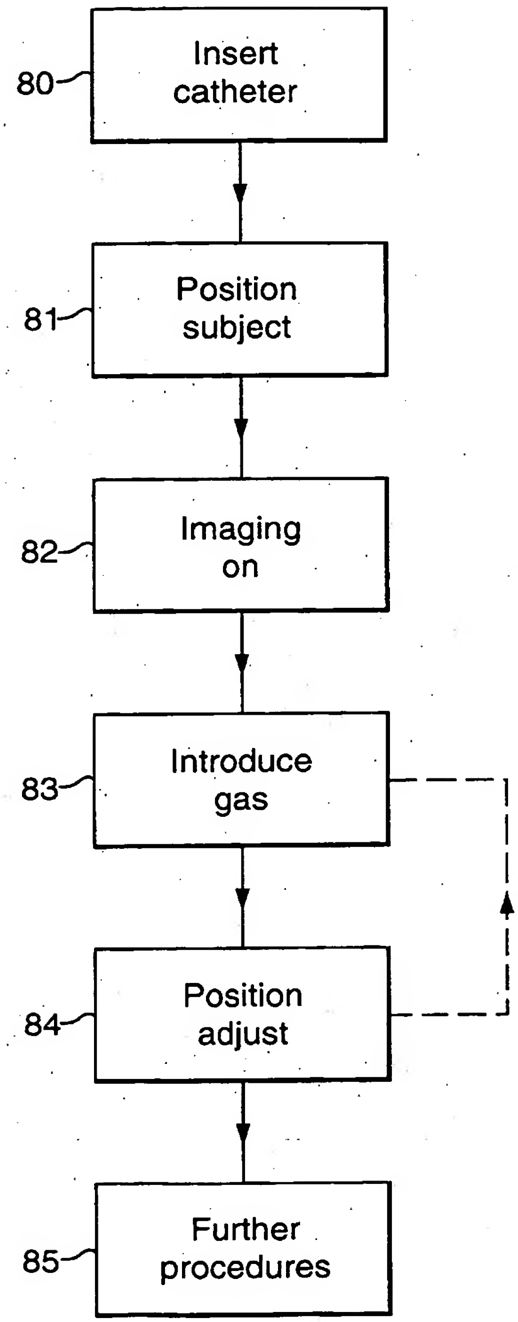


Fig.4.


80
Insert catheter
81
Position subject
82
Imaging on
83
Introduce gas
84
Position adjust
85
Further procedures

INTERNATIONAL SEARCH REPORT

tional Application No
PCT/GB 02/01915

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01R33/28 A61B5/055

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01R A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE, INSPEC, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CRÉMILLIEUX Y ET AL: "A Combined 1H Perfusion/3He Ventilation NMR Study in Rat Lungs" MAGNETIC RESONANCE IN MEDICINE, BERKELEY, US, vol. 41, 1999, pages 645-648, XP002143614 * section "NMR Methods" *	1-4,6-8, 10-13, 18-22
Y		14,15

Y	US 5 675 254 A (DOLINSEK JANEZ ET AL) 7 October 1997 (1997-10-07) claim 11	14

Y	EP 0 955 554 A (PICKER INT INC) 10 November 1999 (1999-11-10) claims 1-10	15

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
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Date of the actual completion of the international search	Date of mailing of the international search report
18 June 2002	26/06/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Skalla, J

INTERNATIONAL SEARCH REPORT

International Application No
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